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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,706	10/29/2003	Katherine A. Galvin	MPI99-283P1RCN1M	8515

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/696,706	GALVIN ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50,51,80 and 81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 50, 51, 80 and 81 are pending in the specification.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 6/26/06 is acknowledged. The traversal is on the ground(s) that a search claims reciting SEQ ID NO: 1-3 would not be burdensome because SEQ ID NO:1 and 3 encodes the polypeptide of SEQ ID NO:2. This argument is persuasive. Accordingly, claims 50, 51, 80 and 81 are examined with regard to all sequences (SEQ ID NO:1-3).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 50, 51, 80 and 81 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

Claims 50, 51, 80 and 81 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims are drawn to a method for identifying a compound capable of modulating an endothelial cell activity by contacting an endothelial cell which expresses a polypeptide which is 95% identical to SEQ ID NO:2 or encoded by a polynucleotide which is at least 95% identical to SEQ ID NO:1 or 3 with a test compound and assaying the ability of the compound to modulate the expression of the polypeptide, wherein the endothelial cell activity includes cell proliferation, cell migration or expression of cell surface adhesion molecules. The

prior art teaches the polypeptide having SEQ ID NO:2 is GPCR 4941, which was cloned as sequence related to growth hormone secretagogue receptor (GHS-R) which is an orphan receptor (has no known ligand or function; it was named GPR39 in the reference. See McKee et al (1997) Genomics 46: 426-434. This reference concluded with the observation that the ligand and the function of the GPR39/GPCR 4941 needed to be determined. See Abstract and final paragraph of reference. Applicants did little more than speculate that GPCR 4941 molecules "may be signal transduction proteins" (p. 9, lines 24-25). While Applicant demonstrates that the expression of GCPR 4941 is up-regulated in a number of types of ovarian cancers, there is simply no demonstration of a causal relationship between GPPR 4941 gene expression or polypeptide activity and ovarian cancer or any of the very many other disorders taught in the specification. Likewise, the mere observation that said polypeptide is up-regulated in proliferating HUVEC cells does not necessary mean there is a causal relationship between the expression of said protein and endothelial cell proliferation. Moreover, the specification also fails to teach or given working example what specific function said polypeptide has in any of the endothelial cell activity including cell proliferation, migration or cell surface adhesion molecule. Given the lack of known function for GPCR 4941 and the lack of causal relationship between it and any endothelial cell activity, there is no specific, credible utility for any compound that is found to modulation GPCR 4941 nucleic acid expression or GPCR 4941 polypeptide activity. Consequently, there is no specific, credible utility for a method of identifying such a compound. The skilled artisan would have to undertake a substantial amount of work to determine the function of GPCR 4941 and if its expression plays any role in the endothelial cell specific activity as recited in claim 51, in order to ascertain a function for such a compound. The claimed

invention is not in a readily available form; instead, further experimentation on GPCR 4941 and its biological function and role in endothelial cell activity would be required before the claimed method could be used.

Claim Rejections - 35 USC § 112

Claims 50, 51, 80 and 81 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The claims are further rejected for lack of enablement for reasons below.

The following factors have been considered in formulating this rejection (In re Wands, 858F.2d 731, 8 USPQZd 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior ad, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The nature of the invention is a method for identifying a compound capable of modulating any endothelial cell activity by contacting an endothelial cell which expresses a polypeptide which is 95% identical to SEQ ID NO:2 or encoded by a polynucleotide which is at least 95% identical to SEQ ID NO:1 or 3 with a test compound and assaying the ability of the compound to modulate the expression of the polypeptide.

The breadth of the claims is rather broad. The claim encompass identifying a compound modulating any endothelial cell activity in cells express a polypeptide which is 95% identical to either the GPCR 4941 polypeptide or nucleic acid encoding said polypeptide.

An analysis of the prior art as of the effective filing date of the present application shows, as discussed above, GPCR 4941 was cloned in 1997 by McKee et al as a sequence related to an orphan receptor called growth hormone secretagogue receptor (GHS-R). This orphan receptor is speculated to respond to an undiscovered hormone involved in the pulsatile release of GH. See p. 426, second column, lines 4-6. GPCR4941 /GPR39 was cloned from human genomic DNA under low stringency hybridization conditions. The ligand-binding and functional properties of GPR39 were not determined in this reference. See p. 433, second column, lines 5-13. The relative skill of those in the art of assays for determining endothelial cell function is high. The area of the invention is unpredictable because it is not known what endothelial cell function said polypeptide is responsible for, and how to use said identified compound specifically.

The present specification provides little direction or guidance to support the claimed invention. The specification describes a very broad range of cardiovascular disorders and tumorigenic disorders (see pp. 10-1 1) that may be treated by the compounds identified by the claimed method. As discussed above, there is no disclosure of the biological function of GPCR 4941 nor is there any disclosure of aberrant gene expression of GPCR 4941 or GPCR 4941 polypeptide activity being causal in any of these disorders. While the examples indicate that GPCR 4941 expression is up-regulated in several types of ovarian tumors, some breast tumors, lung tumors and glioblastomas and may correlate with pathogenesis of atherosclerosis (see Ex. 2 and 3), such correlations do not indicate a causal relationship between the up-regulation of GPCR 4941 and the disorder. Moreover, the specification also fails to teach or given working example what specific function said polypeptide has in any of the endothelial cell activity including cell proliferation, migration or cell surface adhesion molecule. The specification fails

demonstrate that the up-regulated expression of said polypeptide in proliferating cells is results in cell proliferation. Therefore, it is entirely unknown if a compound which modulates with the nucleic acid expression could possibly modulating endothelial cell activity such as cell migration, proliferation or expression of cell surface molecules.

The teaching of the specification is limited. While the specification teaches a GPCR4941 encoded by SEQ ID NO:2, the specification does not disclose other polypeptides that have 95% identity with said polypeptide. The specification also fails teach what type of cell, or if endothelial cell expresses polypeptides having 95% identity with SEQ ID NO:2 or encoded by nucleic acid having 95% identity with SEQ ID NO:1 or 3. As such, whether a compound that modulate the expression of polypeptide 95% having 95% identity with SEQ ID NO:2 or encoded by nucleic acid having 95% identity with SEQ ID NO:1 or 3 can modulate endothelial cell activity is unpredictable.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to teach how to use the claimed method. One of skill in the ad would have to undertake a very substantial amount of experimentation in order to use the method. First, one must ascertain the biological function of GPCR 4941 . Second, one must determine if the up-regulated gene expression of GPCR 4941 is the cause of any endothelial cell activity or what are those activity. Third, one must determine if any endothelial cell expresses a polypeptide having 95% identity with SEQ ID NO:2 or encoded by nucleic acid having 95% identity with SEQ ID NO:1 or 3, and whether such polypeptide is involved in any endothelial cell activity. Fourth, if any compound which modulates either the gene expression of said polypeptides has any patentable utility. Since

neither the prior art nor the present specification provides the answer to all of the questions, it would require a large quantity of trial and error experimentation by the skilled artisan to answer them.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation to practice the method as claimed. Therefore, the claims are not enabled.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CELINE QIAN, PH.D.
PRIMARY EXAMINER

Celine X Qian Ph.D.